95% CI; $P < 0.001$) increased the risk of amputation. In the matched control cohort, burn etiology comprised 25 (57%) of the injuries (11 APs and 14 controls). Of those admitted for nonburn mechanisms, 4 APs and 5 NAPs had infectious processes (20%); 2 in each group with frostbite (9%), 2 APs and 1 NAP with purpura fulminans (7%), and 2 APs with 1 NAP had other conditions. There were 3 deaths in the AP and 2 in the NAP groups. Two of the older patients died of non–ST-elevation myocardial infarction complications during their hospitalization. Of 44 patients, 12 (27%) had upper and lower extremity amputations. Of 66 total amputations performed, 30 (46%) were upper extremity only, 24 (36%) were lower only, and 12 (18%) were in both. The age (48 ± 22 versus 44 ± 20 years; $P = 0.46$) and %TBSA (25 ± 55 versus 22 ± 25; $P = 0.67$) of the 2 groups were similar; however, the APs had a longer length of stay (42 ± 22 versus 21 ± 21 days; $P < 0.002$) compared to NAPs. The AP developed more infections such as sepsis, urinary tract infections, pneumonia, and gangrene (16 [73%] versus 6 [27%]; $P < 0.002$) and subsequently required more antibiotics (21 [68%] versus 10 [32%]; $P < 0.0002$).

CONCLUSIONS: Prognosticating factors such as injury severity and stress, older age, comorbidities, intensive therapy requirements, and infectious complications increase the risk for upper and lower extremity amputations.

Mechanical Stretch Preconditioned Adipose-derived Stem Cells Improve Impaired Wound Healing by Inducing Macrophage M2 Polarization

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BACKGROUND: Uncontrolled inflammatory response during wound healing leads to aberrant repair. Administration of cells/cell factors capable of screwing polarized macrophages toward the anti-inflammatory M2 has shown a favorable prospect to the treatment of inflammatory diseases.[1] Studies have reported that adipose-derived stem cells (ADSCs) have an immunoregulatory effect and improve cutaneous wound healing, but the therapeutic effect on impaired wound still needs to be enhanced. Previously, we found that mechanical stretch preconditioning could enhance the cellular viability and secretion function of ADSCs in vitro. However, it is unknown whether mechanical stretch preconditioning could enhance the immunoregulatory effect of ADSCs on impaired wound healing. The aim of our study is to investigate whether mechanical stretch preconditioned ADSCs could regulate macrophage polarization and improve impaired wound healing.

MATERIALS AND METHODS: Mouse ADSCs were obtained and divided into 2 groups: stretched ADSCs (ms-ADSCs) and nonstretched ADSCs (con-ADSCs). Cyclic mechanical stretch (10%, 12 hours, 0.5 Hz) was applied by the Flexcell FX-5000 system. The ms-ADSCs or con-ADSCs were cocultured with murine macrophage RAW264.7 cells with/without LPS or interleukin (IL)-4 stimulation for 24 hours, respectively. Then M1 markers (iNOS, tumor necrosis factor [TNF]-α, and IL-6) and M2 markers (Arg-1, CD2016, and IL-10) were determined by reverse transcription-quantitative polymerase chain reaction. Eight-millimeter diameter full-thickness excision wounds were made on the dorsal skin of db/db diabetic mice as a delayed wound healing model. Intradermal injections of 5×10^6 ms-ADSCs or con-ADSCs around wound margins were conducted at 2 days postinjury. Histologic studies were performed, and the proinflammatory cytokines (TNF-α, IL-1β, and IL-6) and prohealing cytokines (IL-10, VEGF, and insulin-like growth factor-1) were observed by immunohistochemistry. The M1/M2 polarization in vivo was further evaluated by iNOS/Arg-1 immunofluorescence via confocal microscopy.

RESULTS: The iNOS, TNF-α, and IL-6 mRNA levels of RAW264.7 cells were significantly reduced after coculture with ms-ADSCs than con-ADSCs, whereas the Arg-1, CD2016, and IL-10 mRNA levels reversed. In addition, histologic studies and immunohistochemistry showed that ms-ADSCs treatment significantly accelerated impaired wound healing and reduced inflammatory response characterized with lower expression of TNF-α, IL-1β, and IL-6 and higher expression of IL-10, VEGF, and insulin-like growth factor-1 in the wound. Besides, ms-ADSCs treatment led to a decrease of M1/M2 ratio based on the iNOS/Arg-1 immunofluorescence.

CONCLUSION: Mechanical stretch preconditioning enhanced the ADSCs-guided macrophage polarization from M1 to M2, and mechanical stretch preconditioned ADSCs improved impaired wound healing.

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Nipple-sparing Mastectomy With Immediate Neurosensitization of the Nipple Areola Complex

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BACKGROUND: Nipple-sparing mastectomy (NSM) has been proven to be an oncologically safe technique for treatment of breast cancer. Patients' primary dissatisfaction with the procedure is the loss of nipple areola complex (NAC) sensation. Experience in hand surgery have shown nerve allograft as a successful conduit for nerve repair and good sensory return. Recently, nerve allografts have been employed to provide sensate autologous flaps in breast reconstruction to connect intercostal nerves to sensory nerves of autologous flaps. Expanded and novel use of nerve allografts has the potential to preserve NAC sensation after NSM.

MATERIALS AND METHODS: At the time of NSM, the fourth lateral cutaneous intercostal nerve is identified as it leaves the chest wall and into the breast tissue. At least 1 cm of the nerve is dissected from the breast tissue and preserved. The nerve stump is connected to a 7 cm nerve allograft using 8-0 nylon. To reach the NAC, a second 5–7 cm graft is connected to distal end of the graft. Breast reconstruction then proceeds, and once completed, before skin closure, the nerve allograft is routed over vascularized tissue. The individual axons at the end of the allograft splayed out, and individual axons are sutured into the deep surface of the NAC using 8-0 nylon. Follow-up sensation evaluation is done at 3 months, 6 months, 1 year, and 2 years. Semmes–Weinstein monofilaments and the Acroval Neurosensory and Motor Testing System were used to evaluate patient sensation.

RESULTS: A total of 47 patients underwent NSM and immediate breast reconstruction with direct connection of the NAC. Average age of patients was 47. Five patients were unilateral mastectomy and 42 were bilateral for a total of 89 breasts with 55 breasts being prophylactic. Eleven of the patients had neoadjuvant chemotherapy. Twelve patients underwent autologous reconstruction and 35 underwent expander placement with acellular dermal matrix. No complications reported. At 3-month follow-up for neurotized patients, SWMF 6.65 was felt 31.88% of the time at various breast locations, and SWMF 2.83 was felt 15.22% of the time. Six-month follow-up indicates that sensation is positively progressing for neurotized patients who showed early signs of sensory function.

CONCLUSION: Sensation preservation after NSM is a viable option and best performed at the time of mastectomy. Connecting the fourth lateral cutaneous intercostal nerve to the NAC would allow for return of sensation which is often lost. Coordination with breast surgeon is paramount for the identification and preservation of target nerves and success of the procedure. Use of allograft allows the nerve to be connected to the NAC without additional donor site morbidity. The procedure is technically difficult but feasible and does not add increased complication to breast reconstruction. Three-month and 6-month follow-up results indicate that breast sensation is more likely and significantly quicker in neurotized patients. One-year follow-up sensation testing will provide further evidence for the return of sensory function.